REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 54-55, 57-58, 61-63 and 64-83 are pending in the present application. Claims 54, 55, 57, 58, 61-63 and 64-71 have been amended to address the formal matters raised in the outstanding Official Action. Claims 72-83 have been added. Support for claim 72 may be found in the present specification at page 5, lines 33-34; and page 6, lines 9-11. Support for claims 73 to 80 may be found in the present specification at page 19, line 21 to page 21, line 12 and in Figure 1. Claims 81-83 are supported by the present specification at page 21, line 33 to page 22, line 16.

In the outstanding Official Action, claims 54-58, 61-63 and 65-70 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the enablement requirement. The rejection is respectfully traversed.

In imposing the rejection, the Official Action alleges that the specification discloses that only cultures employing 1,000 IU/ml IFN resulted in functional dendritic cells. Additionally, the Office Action contends that all disclosed cultures employed 500 IU/ml GM-CSF. Accordingly, the Official Action concludes that the use of 500 IU/ml GM-CSF in the claimed method is essential.

However, applicants respectfully note that page 6 of the present specification teaches that IFN shall generally be present in the culture medium at a final concentration greater than 100 IU/ml. The specification expressly teaches that type I IFN may be present in preferred ranges of 100-10,000 IU/ml, 400-10,000 IU/ml, 500-2,000 IU/ml, particularly 1,000 IU/ml. The present specification also plainly states that the GM-CSF may be preferably used at a concentration in a range of 250-1,000 IU/ml (page 5, lines 33-34).

Thus, the present specification does not teach that only cultures employing 1,000 IU/ml IFN and 500 IU/ml GN-CSF result in dendritic cells. While it is true that the examples in the present specification may utilize these amounts, the specification certainly does not teach that these are the only amounts that may be used to practice the claimed invention.

It is also true that cultures containing 100 IU/ml of type I IFN may not result in functional dendritic cells. However, the specification takes this into account and teaches one skilled in the art that amounts "greater than" 100 IU/ml should be utilized (page 6, lines 5-10). The claims go further, by requiring that at least 400 IU/ml be used.

Thus, not only does the present specification teach one skilled in the art that particular ranges of concentration levels of IFN and GM-CSF may be used, the present specification also

teaches one skilled in the art amounts that may not be suitable for practicing the claimed invention.

As a result, applicants believe that the present disclosure does enable the claimed invention.

In this regard, the Examiner is respectfully reminded that MPEP §2164.02 states that the presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it may be a factor to consider. Rather, to make a valid rejection, one must evaluate all the facts in evidence and say why one would not expect one skilled in the art to be able to extrapolate that one example across the entire scope of the claims.

Accordingly, applicants respectfully submit that the Office Action fails to provide any evidence that why show why one skilled in the art would not expect to be able to extrapolate the examples provided by the applicant across the entire scope of the claims.

Rather, in imposing the rejection, the Official Action notes that MPEP §2164.03 states that physiological processes are generally considered to be unpredictable. While it is true that chemical reactions and physiological activities may be less predictable than mechanical and electrical elements, applicants note that MPEP §2164.03 does not relieve the Patent Office of its burden in showing that a claimed invention is not enabled.

Moreover, the Examiner is respectfully reminded that it is a well founded principle that any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed.

As a matter of law, the expressed teaching of the patent specification cannot be controverted by mere speculation and unsupported assertions on the part of the Patent Office. As stated by the Court of Customs and Patent Appeals in the case of *In re Dinh-Nguyen and Stanhagen,* 181 USPQ 46 (CCPA 1974):

> Any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed. 181 USPQ at 47.

Such a standard must be applied with great care when the Examiner's conjecture is contrary to the teachings of the specification.

As the Office Action does not present any evidence to the contrary the claimed concentration ranges are not enabled, applicants respectfully submit that the Patent Office fails to satisfy its burden in showing that the present disclosure is not enabling for the claimed concentration ranges recited in the claims.

As to the claimed ranges, Figure 3 of the present specification compares the effects of different doses of type I IFN, in particular 1,000 IU/ml, 500 IU/ml and 100 IU/ml, added

together with 500 IU/ml of GM-CSF. The concentrations of 500 and 1,000 IU/ml of type I IFN can lead to cells expressing characteristic DCs surface makers CD86 and CD80, wherein the concentration of 100 IU/ml of type I IFN does not.

The article of Santodonato et al. ("*Dendritic cells generated from human CD14+ monocytes in the present of type I IFN efficiently stimulate an Epstein-Barr Virus-specific CD 8+ T cell response*", J. Exp. Med, Vol. 198, number 2, July 21, 2003, 361-367) attached with this amendment for the Examiner's convenience shows that DCs obtained within 3 days in the presence of GM-CSF 500 IU/ml and consensus IFN-alpha 1,000 IU/ml (a synthetic type I IFN provided by Amgen) and pulsed with EBV peptides are able in vitro to stimulate the expansion of EBV-specific T cells and to promote the expansion of memory T cells. When injected into SCID mice transplanted with human PBLs, the peptide-pulsed DC promoted the expansion of CD8+ T cells.

Moreover, other results obtained by the inventors show that IFN concentrations of 10,000 IU/ml can also lead to functional DCs. Lapenta et al., attached herewith ("*Potent Immune response against HIV-1 and protection from virus challenge in hu-PBL-SCID mice immunized with inactivated virus-pulsed DCs generated in the presence of IFN-alpha*", J. Exp. Med, vol. 198, number 2, July 21, 2003, 361-367) contacted for 3 days isolated CD14+ monocytes with 500 IU/ml GM-CSF and either 10,000 IU/ml natural IFN-alpha (Alfaferone: Alfa Wasserman) or 250 IU/ml IL-4

(page 362). Dendritic cells obtained with IFN-DCs and L-4-DCs were pulsed with inactivated HIV and injected to hu-PBL-SCID mice.

The production of anti-HIV1 antibodies was measured, with a less intensive response and lower neutralizing activity after administration of IL-4-DCs than after administration with IFN-DCs. The reaction of CD8+ T cells against HIV-1 was also determined, with a higher response when mice received IFN-DCs. Thus, these results show that IFN-DCs are superior to immature IL-4-DCs in inducing an in vivo cross priming of CD8+ T cells against exogenous HIV antigens. Higher activity of IFN-DCs could be explained by the strong Th1-type of immune response elicited by the cells.

Therefore, applicants consider that the 250-1,000 IU/ml range of GM-CSF concentrations is enabled.

Thus, in view of the above, applicants respectfully submit that the present disclosure is enabling for the claimed concentration ranges.

Claims 55 and 62 were rejected under 35 USC 112, second paragraph for allegedly being indefinite.

Applicants believe that the present amendment obviates this rejection. The claims as identified by the Office Action either have been deleted from the claims or have been further characterized by a Markush group. Thus, applicants respectfully submit that the present amendment obviates this rejection.

Claims 54-58, 61-63 and 65-71 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the written description requirement. This rejection is respectfully traversed.

In imposing the rejection, the Office Action alleged that the phrases "greater than 400 IU/ml" and "wherein IL-4 is absent" introduce new matter into the present disclosure.

As to the phrase "greater than 400 IU/ml", this phrase has been deleted from the claims.

As to the recitation "in the absence of IL-4", the phrase may not be explicitly supported in the specification. However, the comparison of dendritic cells obtained with the process of the claimed invention as compared to dendritic cells obtained with a culture containing IL-4 and GM-CSF implicitly shows that applicants intended a comparison of the cells obtained by the claimed process relative to those obtained in the "absence of IL-4".

The Examiner's attention is also respectfully directed to claim 69 which recites "in the absence of added IL-4", a recitation also implicitly supported by the specification in that the specification discusses the comparison of dendritic cells obtained with the process of the claimed invention as compared to dendritic cells obtained with a culture containing IL-4 and GM-CSF

Claims 56-58, 61-63 and 65-71 were rejected under 35 USC 102(b) as allegedly being anticipated by PAQUETTE et al. This rejection is respectfully traversed.

PAQUETTE et al. discloses a culture of isolated monocytes with a combination of GM-CSF and IFN in order to obtain dendritic cells. Yet the method of the invention differs from that of PAQUETTE et al. in that the method of PAQUETTE et al. involves 7 days of culture whereas that of the claimed invention recites that the cells are obtained after a maximum of 3 days.

As PAQUETTE et al. fails to disclose or suggest recovering cells after a maximum of 3 days of culture, applicants believe that PAQUETTE et al. fail to anticipate or render obvious the claimed invention.

Claim 61 was rejected under 35 USC 112, second paragraph, for allegedly being indefinite. However, claim 61 has been amended so it is now dependent on claim 54. Thus, applicants believe that claim 61 is definite to one skilled in the art.

Claims 54-58, 62 and 68-71 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the written description requirement.

In imposing the rejection, the Office Action alleged that the present disclosure does not satisfy the recitations of "isolating said cells after culturing said cells for 3 days", or "isolating said dendritic cells after 3 days of culture".

Applicants note that the specification teaches the "recovery" and "collection" of cells after 3 days at page 18, lines 19-24 and page 25, lines 10-14 in the present specification.

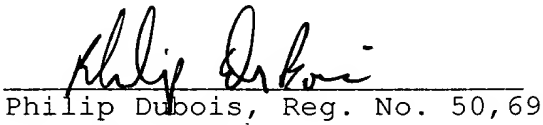
Accordingly, applicants respectfully submit that the present disclosure satisfies the recitations of "isolating said dendritic cells after 3 days of culture" or "isolating said cells after 3 days of culture". Nevertheless, in the interest of advancing prosecution, the claims have been amended to recite the recovery or collection of the cells.

In view of the present amendment and the foregoing Remarks, therefore, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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